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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/871,367 | 05/31/2001 | Katrin Kriwet | 4-30724A | 1754 |

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NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

| EXAMINER | |
|---|---|
| KIM, VICKIE Y | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1618 | |

DATE MAILED: 05/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/871,367 | KRIWET ET AL. | |
| | Examiner | Art Unit | |
| | Vickie Kim | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *14-41* is/are pending in the application.

4a) Of the above claim(s) *14,16,18,20,21,23,25,27,29,31 and 33-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,17,19,22,24,26,28,30,32 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of Application*

1. Acknowledgement is made of amendment filed January 05, 2004. Upon entering the amendment, the claim 15 is amended.

2. The claims 14-41 are pending. The elected invention of claims 15, 19, 22, 24, 26, 30 and 32 are presented for the examination(sodium chloride:elected species) and the non-elected invention of claims 14, 16, 18, 20, 21, 23, 25, 27, 29, 31 and 33-40 are withdrawn from consideration.

### *Response to Arguments*

3. Applicant's arguments with respect to claims 15, 19, 22, 24, 26, 30 and 32 have been considered but are moot in view of the new ground(s) of rejection because the scope of the claims are changed. New limitation(i.e. water in an amount of from 0 to about 10%) is added.

### *Claim Rejections - 35 USC §102*

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claim 15, 19, 22, 24, 26 and 30 are rejected under 35 U.S.C. 102(b) as anticipated by Natsuyama et al( JP 08-133979).

The claims are drawn to a composition in the form of an ointment for topical administration of 33-epi-chloro-33-deoxy-ascomycin, wherein the composition comprises 33-epi-chloro-33-deoxy-ascomycin and a carrier vehicle comprising (i) means to retain water in the outer skin layer, and (ii) means to hinder water evaporating from the skin(e.g. hydrocarbons such as paraffin, petrolatum, etc) .

JP'979 teaches a topical composition that provides good permeation and local applicability, wherein the composition comprising cyclosporine or 33-epi-chloro-33-deoxy-ascomycin as an active agent; oleypl alcohol, propylene glycol, and liquid paraffin to make semisolid formula such as ointment, see abstract and examples. Especially a patented composition(example 31 or 32 at page 5) comprises an active agent(e.g. cyclosporine), oleyl alcohol(fatty alcohol), paraffin, liquid paraffin or Vaseline(=petrolatum), isopropyl myristic acid(fatty acid), and propylene glycol to make ointment.

As to claim 30, JP'979 teaches 0.05-20% of 33-epi-chloro-33-deoxy-ascomycin(active agent and preferred species, see paragraph 12).

As to claim 32, JP'979 teaches 15-99.35% of propylene glycol , see paragraph 14.

Although JP'979 does not explicitly teach about the role of propylene glycol, any ordinary skilled artisan would have been reasonably expected the role of propylene glycol as water retainer because propylene glycol is well known in the art* as water binder(humectant) and retains water to keep the skin moist, (see extrinsic evidence enclosed in PTO-892*, for example, US6322829 teaches inherent feature of

humectant(or water binder) that retains water(e.g. glycols such as propylene glycol, sodium chloride) . Thus, the limitations required by instant claims are inherently met , wherein propylene glycol retains water to keep the skin moist when propylene glycol is applied topically into the skin surface.

All the critical elements required by the instant claims are well taught in the cited reference and thus, the claimed subject matter is not patentably distinct over the prior art of the record. Although JP'979 does not explicitly show a example composition containing 33-epi-chloro-33-deoxy-ascomycin, JP'979 clearly suggests 33-epi-chloro-33-deoxy-ascomycin as an active agent, equivalent to cyclosporine(see claim 1, paragraph 12 and abstract) and thus, the claimed subject matter is clearly envisioned.

Thus, all the claims are properly included in this rejection and they are not considered to be patentably distinct over the prior art of the record.

6. Claim 15, 19, 22, 24, 26 and 30 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Mrowietz et al(1998).

The claims are drawn to a composition in the form of an ointment for topical administration of 33-epi-chloro-33-deoxy-ascomycin, wherein the composition comprises 33-epi-chloro-33-deoxy-ascomycin and a carrier vehicle comprising (i) means to retain water in the outer skin layer, and (ii) means to hinder water evaporating from the skin(e.g. hydrocarbons such as paraffin, petrolatum, etc) .

The claims 24 and 26 require a fatty alcohol.

Mrowietz et al teach a topical composition containing SDZ ASM 981 as an active agent for treating psoriasis, see abstract. It is noted that SDZ ASM 981 is 33-epi-chloro-33-deoxy-ascomycin(same compound), both are same compound with different chemical name, see figure 1 at page 993 and also see registry file (enclosed in PTO-892).

Especially, Mrowietz et al further teach a topical composition is an ointment form which contains SDZ ASM 981 (0.3% and 1%) in an ointment base. The said ointment base comprises eucerinum anhydricum(51%), hexylene glycol(30%), miglyol(11%) and oleylalcohol(7.5%), see last paragraph at page 992 and 1st paragraph at page 993. It is well known in the art* that Eucerinum anhydricum is a paraffin derivative(hydrocarbon) that hinders water evaporating from the skin and hexylene glycol is a humectant that inherently retains water in the outer skin, as well as evidenced by numerous documents , see *extrinsic evidence enclosed in PTO-892. Thus, all the critical elements are well taught in the cited reference and the claimed subject matter is not patentably distinct over the prior art of the record.

*-- US6322829 teaches inherent feature of humectant(or water binder) that retains water(e.g. glycols such as propylene glycol, sodium chloride) .

--US 5981464 teaches a humectant utilized in cosmetic/pharmaceutical field(e.g. glycols such as hexylene glycol, propylene glycol, etc)

--Allergy elimination.., teaches Eucerinum anhydricum is a paraffin derivative.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 17, 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mrowietz et al(1998) in view of HE et al(US 5981464) and McGlynn et al(US6322829).

Mrowietz et al's teaching is mentioned immediately above in 102 rejection.

Applicants' claims are different from Mrowietz et al because the claims require inorganic salt.

Although Mrowietz et al do not explicitly teach about the role of hexylene glycol, any ordinary skilled artisan would have been reasonably expected the substitution of hexylkene glycol with inorganic salt because the role of hexylene glycol as water retainer(*see also dictionary: the definition of "humectant": a substrate added to antother substance to keep it moist) is well known in the art and inclusion of hexylene glycol for said purpose is routinely practiced in the cosmetic/pharmaceutical product. The examiner's allegation can be evidenced by extrinsic supporting documents.

He(US 464) teaches that hexylene glycol and propylene glycol are effective humectants and functionally equivalent to each other.

McGlynn et al(US'829) teaches about humectant that retains water. US'829 particularly teaches sodium chloride, propanediol, propylene glycol are effective humectant.

In light of specification, inorganic salt refers to sodium chloride, see page 4, line 11. Thus, when these references are taken together, it would have been obvious to one of ordinary skill in the art to substitute hexylene glycol with inorganic salt such as sodium chloride to retain the water in the composition that eventually left in the skin surface so that water(moist) can be retained in the skin to the skin moist.

The minor variations(e.g. dose, route of administration, etc), can be titrated in order to determine the most successful outcome and it is considered well within skill of ordinary artisan.

One would have been motivated to make such substitution, with reasonable expectation of success because it is always desirable to have extended selection for the basic ingredients to improve patient's compliance by enhancing patient satisfaction and to reduce manufacturing cost by increasing the selection option(sodium chloride is easily obtained).

The techniques and skills required for making such substitution is conventional knowledge or well within the skills of ordinary artisan.One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities, and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

9. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Natsuyama et al( JP 08-133979).

JP'979 teaches a topical composition that provides good permeation and local applicability, wherein the composition comprising cyclosporine or 33-epi-chloro-33-deoxy-ascomycin as an active agent; oleypl alcohol, propylene glycol, and liquid paraffin to make semisolid formula such as ointment, see abstract and examples. Especially a patented composition(example 31 or 32 at page 5) comprises an active agnet, oleyl alcohol, paraffin or vaselin, and propylene glycol to make ointment.

As mentioned above, propylene glycol is well known water binder(humectant) and retains water to keep the skin moist.

Applicants' claims are different from Mrowietz et al because the claims require inorganic salt.

McGlynn et al(US'829) teaches about humectant that retains water. US'829 particularly teaches sodium chloride, propanediol, propylene glycol are effective humectant.

One would have been motivated to make such substitution, with reasonable expectation of success because it is always desirable to have extended selection for the basic ingredients to improve patient's compliance by enhancing patient satisfaction and to reduce manufacturing cost by increasing the selection option(sodium chloride is easily obtained).

The techniques and skills required for making such substitution is conventional knowledge or well within the skills of ordinary artisan.One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities, and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

***Conclusion***

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vickie Kim whose telephone number is 571-272-0579. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Chris Low be reached on 571-272-0953. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

VICKIE KIM
PRIMARY EXAMINER

Vickie Kim
Primary Patent Examiner
April 30, 2005
Art unit 1618